DEC 1 8 2002

K022713

A. The Summary shall contain sufficient detail to provide an understanding of the basis for a determination of substantial equivalence.

A.1. ***Submitter's Name:***

Diagnostic Hybrids, Inc.
350 West State Street
Athens, OH 45701
Attention: James L. Brown
740-593-1784
Date of preparation: July 1, 2002

A.2. ***Name of the Device:***

Trade Name: DFA Respiratory Virus Screening & ID Kit
Common Name: Direct Fluorescent Antibody test kit for the identification of 7 common respiratory viruses (Adenovirus, Influenza A, Influenza B, Respiratory Syncytial Virus and Parainfluenzas 1, 2 and 3) in patient specimens and cell cultures.

A.3. ***Identification of the Predicate Devices:***

The predicate device(s) to which substantial equivalence is being claimed is the

(1) Bartels Viral Respiratory Screening and Identification Kit

and

(2) Diagnostic Hybrids, Inc. IFA Respiratory Viruses Screening and Identification Kit

It must be noted that this second device is identical to the first and is manufactured by Trinity Biotech, Plc and that Diagnostic Hybrids, Inc. simply distributes these kits under the DHI label.

Manufactured by Trinity Biotech, Plc
IDA Business Park
Bray, County Wicklow
Ireland

This predicate device(s) (a copy of the product inserts are included in Appendix 1 and 2) provides Indirect Fluorescent Antibody (IFA) reagents to screen for and identify the same 7 common respiratory viruses but uses *non*-labeled, specific murine monoclonal antibodies. It relies on secondary, fluorescein-labeled, goat-antimouse polyclonal antibodies for detection of the virus-specific, murine monoclonals after they have reacted with their respective viral antigens.

A.4. ***Description of the premarket notification device:***

The subject device consists of a series of reagents that are used to screen for and identify 7 common respiratory viruses using murine monoclonal antibodies *directly* labeled with fluorescein (Direct Fluorescence Assay or DFA) and which are specific for antigenic determinants found on each virus. It is this difference,

DFA *vs.* IFA, that distinguishes the premarket notification device from the predicate device.
The advantage that DFA offers over IFA is that DFA assays can be performed in less than half the time and with fewer reagents and steps required for the IFA. As in the predicate test, the DFA test uses Evans Blue in the antibody solutions to counterstain the cells in the specimen or cultured cells to provide greater contrast for visualizing fluorescence, if present.
All the solutions (except the Wash Concentrate) are contained in dropper bottles not requiring pipetting of specific volumes to facilitate the performance of the assay.

The subject device provides the following materials:

Respiratory Virus DFA Screening Reagent: A solution containing a mixture of fluorescein-labeled murine monoclonal antibodies directed against antigenic determinants of each of 7 of the common respiratory viruses.
Seven Individual DFA Solutions of the same fluorescein-labeled murine monoclonal antibodies as in the above Screening Reagent but each solution contains only antibodies specific for one of the 7 viruses, i.e., Adenovirus, Influenza A, Influenza B, Respiratory Syncytial Virus and Parainfluenzas 1, 2 and 3.
Antigen Control Slides: Slides containing 8 wells with infected and non-infected cells. Each of the 7 positive wells is identified as to the virus infection, i.e., Adenovirus, Influenza A, Influenza B, Respiratory Syncytial Virus and Parainfluenzas 1, 2 and 3. The negative well contains uninfected cells.
Normal Mouse Gamma Globulin DFA Reagent: A solution of fluorescein-labeled murine gamma globulin, unreactive with any of the 7 respiratory viral antigens.
Wash Solution Concentrate: A 40X concentrate of a non-ionic detergent (Tween 20) in a buffered, stabilized solution.
Mounting Fluid: An aqueous, buffered, stabilized solution of 60% glycerol.

The subject device is used as follows:

Direct Testing of Patient Specimens: The specimen (aspirates, washes or swabs from the nasopharyngeal area) is diluted in transport medium, centrifuged, the supernatant set aside for the cell culture step (below) and the pellet of cells washed and resuspended in a small volume of phosphate buffered saline (PBS). A drop of the cell suspension is added to each well of a 2-well and an 8-well microscope slide and air dried. Each slide is then immersed in acetone to fix the cells and air dried.

A drop of the *DFA Screening Reagent* is added to the fixed cells of one well of the 2-well slide and to each well of the 8-well *Antigen Control Slide*. A drop of the *Normal Mouse Gamma Globulin DFA Reagent* is added to the remaining well

of the 2-well slide. The slides are then placed in a covered, humidified chamber at 35° to 37°C for 15-30 minutes. During the incubation, the fluorescein-labeled monoclonal antibodies bind to their specific viral antigens in the infected cells (if present) from the nasopharynx and to the infected cells in the wells of the *Antigen Control Slide*. The cells are then rinsed using a 40X dilution of the *Wash Solution Concentrate* to remove any unbound antibody. A drop of *Mounting Fluid* is added to each well, covered with a coverslip and examined using a fluorescence microscope.

If no fluorescence is seen in the *DFA Screening Reagent*-well of the 2-well slide or the uninfected well of the *Antigen Control Slide* and fluorescence is seen in all the positive wells of the *Antigen Control Slide*, the specimen is reported as negative for these respiratory viruses and the negative result is confirmed by culture.

If fluorescence is seen in the *DFA Screening Reagent* well of the 2-well slide and fluorescence is seen in all the positive wells of the *Antigen Control Slide*, and if no fluorescence is seen in the *Normal Mouse Gamma Globulin DFA Reagent* well and none in the negative well of the *Antigen Control Slide*, the patient result is positive for one of the 7 respiratory viruses.

In order to determine which of the 7 viruses is present in the specimen, the 8-well slide with the patient specimens (above) is then stained by adding one drop of each of the specific virus *Individual DFA Solutions* of monoclonal antibodies to the respective, virus-identified wells and the slide placed in a covered, humidified chamber at 35° to 37°C for 15-30 minutes. A drop of *Mounting Fluid* is added to each well, covered with a coverslip and examined using a fluorescence microscope. The identity of the infecting virus is determined by examining each well; the specific, virus-identified well with the fluorescing cells confirms the identity of the infecting virus. The specimen is reported as positive for the respective respiratory virus.

Cell Culture Testing of Specimens: If using tubes, remove the maintenance medium from the appropriate cell cultures and add 0.2 to 0.5 ml of specimen to cover the monolayers and allow 1 hour for adsorption at 35° to 37°C. Add 2 ml of the appropriate refeed medium and incubate at 35° to 37°C. Examine the monolayers daily for CPE or test for hemadsorption. Once viral infection is evident, remove the medium and scrape and suspend the monolayer in about 0.5 ml of PBS. Add a drop of the suspension to a 2-well slide and an 8-well slide, as above, air dry, fix in acetone and air dry again. Stain and interpret the results as in the above procedure for Direct Testing of Patient Specimens.

If using shell vials with coverslips, remove the maintenance medium from the appropriate cell cultures and add 1 ml of refeed medium; add 0.2 to 0.4 ml of specimen to each vial and centrifuge at 700xg for 1 hour. Incubate at 35° to 37°C and examine daily for CPE or hemadsorption or blind stain using the DFA Screening Reagent at the times previously established by the laboratory. When one of the monolayers is ready to be stained with the *DFA Screening Reagent*, remove the medium and fix the monolayer with acetone; remove the coverslip and allow to air dry. Wash the monolayer with the diluted *Wash Solution*. Stain and

interpret the results as in the above procedure for Direct Testing of Patient Specimens.

A.5. A statement of the intended use of the device.

Intended Use: The Diagnostic Hybrids, Inc. DFA (Direct Fluorescent Antibody) Respiratory Virus Screening & ID Kit is intended for the qualitative detection and identification of the common respiratory viruses, Influenza A, Influenza B, Respiratory Syncytial Virus (RSV), Adenovirus, Parainfluenza 1, Parainfluenza 2 and Parainfluenza 3 directly in prepared patient specimens and in cell cultures following viral amplification. Specimens found to be negative after examination of the direct specimen result must be confirmed by cell culture.

The indication statements differ from those for the predicate device as follows:

1. The predicate device does not allow for detection of Parainfluenza 2 and Adenovirus in prepared patient specimens, a deficiency of the predicate device which has been overcome with the premarket notification device by including the specific antibodies necessary to identify these viral agents in these specimens as well as the clinical information necessary to support and allow for such a claim.

A.6. The differences in technological characteristics between the predicate and premarket notification devices are as follows:

The *premarket notification* device consists of a series of reagents that are used to screen for and identify 7 common respiratory viruses using murine monoclonal antibodies *directly* labeled with fluorescein (DFA) and which are specific for antigenic determinants found on each virus. The *predicate* device provides Indirect Fluorescent Antibody (IFA) reagents to screen for and identify the same 7 common respiratory viruses but uses *non*-labeled, specific murine monoclonal antibodies. It relies on secondary, fluorescein-labeled, goat-antimouse polyclonal antibodies for detection of the virus-specific monoclonals after they have reacted with their respective viral antigens. It is this difference, DFA *vs.* IFA, that distinguishes the *premarket notification* device from the *predicate* device.
The advantage that DFA offers over IFA is that DFA assays can be performed in less than half the time and with fewer reagents and steps required for the IFA. As in the predicate test, the DFA test uses Evans Blue in the antibody solutions to counterstain the cells in the specimen or cell culture to provide greater contrast for visualizing fluorescence, if present.

B. This 510(k) submission includes performance data that shows substantial equivalence between the premarket notification device and the predicate device.

B.1. A brief discussion of the non-clinical tests submitted to permit a determination of substantial equivalence.

For any antibody test for specific viral antigens, it is necessary to demonstrate that the antibodies in the product are specific and do not cross-react with antigens of other viruses or organisms that may be present in the specimen being tested. The

antibodies to the 7 different viruses in the subject product have been tested against 92 potentially cross-reacting organisms (viruses, bacteria and cells) and have been found to yield results which are substantially equivalent to those of the predicate assay, i.e., there was no cross-reactivity found with any of the organisms in the subject assay, demonstrating that it has at least equivalent specificity to that of the predicate assay. The various potentially cross-reacting organisms used in the test were obtained from American Type Culture Collection. These results are included in the Specific Performance Characteristics of the draft product insert included in this submission.

B.2. A brief discussion of the clinical tests submitted to permit a determination of substantial equivalence.

Two study sites (Appendices 1 and 2) were used to test clinical specimens and compare the results of the subject assay to those of the predicate assay using the same prepared direct specimens and specimens amplified in cell cultures. Each study site testing the subject assay used the same protocol and tested the same specimens with the predicate assay. These comparative results demonstrate that the subject assay yields results substantially equivalent to those of the predicate assay. These site studies and results are summarized and presented in the section on Expected Values in the draft product insert as well as in Appendices 1 and 2 which include the specimen data generated by each Study Site.

B.3. The conclusions drawn from the nonclinical and clinical tests that demonstrate the device is as safe, as effective and performs as well or better than the predicate device.

The nonclinical tests which consist of cross-reactivity studies and reagent stability studies were performed at Diagnostic Hybrids, Inc. (DHI) by DHI personnel.

The results from the cross-reactivity studies demonstrated that even at twice the normal concentrations of antibodies used, there was no indication of non-specific binding or cross-reactivity with agents that may be present in specimens being tested.

The clinical evaluations also confirmed this, indicating that the DFA Respiratory Virus Screening & ID Kit yields results substantially equivalent to the predicate kit which has been marketed for more than 7 years.

The reagent stability studies are ongoing and currently permit an outdate of more than 8 months when stored at 2° to 8°C. These studies are being extended and the kits will be outdated for periods as the stability data permit.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

DEC 18 2002

Mr. James L. Brown
Senior Vice President, Chief Operating Officer
Diagnostics Hybrids, Inc.
350 West State Street
Athens, OH 45701

Re: k022713
Trade/Device Name: Diagnostic Hybrids' DFA Respiratory Virus Screening and ID Kit
Regulation Number: 21 CFR 866.3330
Regulation Name: Influenza Virus Serological Reagents
Regulatory Class: Class I
Product Code: GNW
Dated: October 31, 2002
Received: November 1, 2002

Dear Mr. Brown:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known): k022713

Device Name: Diagnostic Hybrids DFA Respiratory Virus Screening and ID Kit

Indications For Use:

The Diagnostic Hybrids, Inc. **DFA (Direct Fluorescent Antibody) Respiratory Virus Screening & ID Kit** is intended for the qualitative detection and identification of the common respiratory viruses, Influenza A, Influenza B, Respiratory Syncytial Virus (RSV), Adenovirus, Parainfluenza 1, Parainfluenza 2 and Parainfluenza 3 in direct specimens and cell cultures. It is recommended that specimens found to be negative after examination of the direct specimen result be confirmed by cell culture.

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The-Counter Use_____
(Per 21 CFR 801.109)

Freddie Lu-Poole

(Division Sign-Off)
Division of Clinical Laboratory Devices

510(k) Number K022713/S1